LETTER TO THE EDITOR

Function of human mineralocorticoid receptor splice variant

V Bähr, C Bumke-Vogt, J Götze, A F H Pfeiffer and S Diederich

Department of Endocrinology, Diabetes and Nutrition, Charité-University Medicine Berlin, Campus Benjamin Franklin, Hindenburgdamm 30, 12200 Berlin, Germany

(Correspondence should be addressed to V Bähr; Email: volker.baehr@charite.de)

In their recent paper, Pascual-Le Tallec *et al.* (1) state that a publication by Bloem *et al.* (2) describes that a mineralocorticoid receptor (MR) splice variant with a 12 bp insertion coding for a protein with four additional amino acids (MR+4) shows no functional difference to the MR without insertion. This evidence is not produced in the publication by Bloem *et al.* or to our knowledge anywhere else. On the contrary Bloem *et al.* propose that the additional four amino acid residues in the DNA binding domain could alter binding to a glucocorticoid response element (GRE) and transcription activation. Because this splice variant shows considerable concentrations in various human tissues (3), we have compared transactivation mediated by MR and MR+4. The plasmid pchMR+12 coding for hMR+4 was created by *in vitro* PCR mutagenesis of pchMR coding for hMR. Transactivation of both variants by aldosterone was analysed in CV-1 cells by measuring firefly luciferase activity of an inducible reporter gene normalised to the activity of constitutively expressed renilla luciferase (Fig. 1) (4).

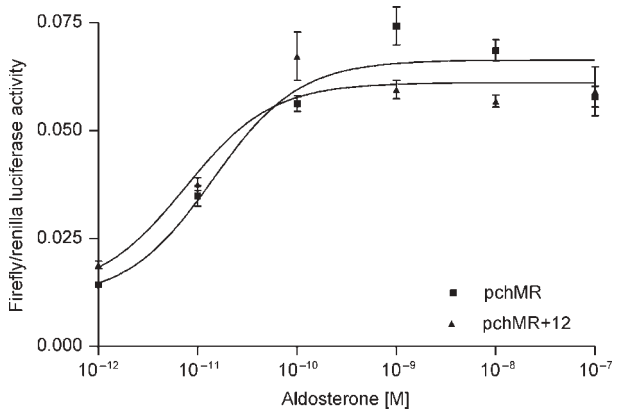

Figure 1 Aldosterone produced a concentration-dependent transactivation of the reporter gene. Half the maximal transactivation (ED_{50}) was achieved near log −11 M aldosterone regardless of whether hMR or hMR+4 was expressed. There was a tendency toward a slightly lower ED_{50} (higher sensitivity) and somewhat weaker transactivation when MR+4 was expressed. The data justify the statement by Pascual-Le Tallec *et al.* (1) that the function of hMR+4 is comparable to that of hMR.

References

1 Pascual-Le Tallec L, Demange C & Lombes M. Human mineralocorticoid receptor A and B protein forms produced by alternative translation sites display different transcriptional activities. *European Journal of Endocrinology* 2004 **150** 585–590.

2 Bloem LJ, Guo C. & Pratt JH. Identification of a splice variant of the rat and human mineralocorticoid receptor genes. *Journal of Steroid Biochemistry and Molecular Biology* 1995 **55** 159–162.

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4 Grossmann C, Scholz T, Rochel M, Bumke-Vogt C, Oelkers W, Pfeiffer AFH, Diederich S & Bähr V. Transactivation via the human glucocorticoid and mineralocorticoid receptor by therapeutically used steroids in CV-1 cells: a comparison of their glucocorticoid and mineralocorticoid properties. *European Journal of Endocrinology* (In press).

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